DETAILED ACTION

Restriction/Election

Applicant's election of Group II, claims 36-58, and the species of gelatine type A (claim 38), lactic acid (claim 42), taurine (claim 47), and chlorhexidine (claim 55) in the reply filed on 12/29/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 33-35 and 59-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected wound dressing and a nonelected method of use of a wound dressing, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/29/2009.

Foreign Priority

Acknowledgement is made that this application is a 371 of PCT/EP04/13575, filed 11/30/2004, and this application claims foreign priority to 2003138256, filed 12/26/2003 in the Russian Federation. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statements (IDS) (4) submitted on 10/06/2006, 12/11/2006, 12/26/2006, and 7/18/2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by

the examiner except where lined through. It is noted that for an entry which has been lined through, the English abstract was enclosed and has been considered although the document as a whole has not been considered.

Specification

Acknowledgement is made of Applicants' amendments to the specification where amendments were filed 6/23/2006, 10/6/2006, and 12/11/2006. These amendments have been entered into the record.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 36 recites the limitation "...and then polyfunctional amino acids and active substances, cross-linking agents, additives and excipients of the dialyzed reaction mixture are added if necessary". It is unclear which of these wound dressing components are necessary, and it is unclear how the skilled artisan would have ascertained the necessity of adding one or more of these components. The specification mentions the potentially necessary addition of active substances (see page

11, lines 25-30), but it remains unclear which formulation components may be necessary, and it remains unclear what objective standards are used to determine said necessity. In the 103 obviousness rejection outlined below, the claim language is interpreted as if the polyfunctional amino acids and active substances, cross-linkage agents, additives and excipients are optional components in the wound dressing production procedure. Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 36, 37, 42, and 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986). Regarding claims 36, 37, 40, and 55, Sparkes et al. teach chitosan based wound dressing material which comprises gelatin and chitosan and a compatible plasticizer (see abstract, in particular). As to claim 42, Example 3 teaches the addition of lactic acid (approximately 2.2% by weight of the total formulation components excluding the aqueous medium which is removed) to chitosan (34.6%), filtration, and the subsequent addition of gelatin (38.2%) in water to the filtrate; after these components are added and incorporated, glycerol (15.3%) in water was added to the mixture from which a wound-adherent (dialyzed) film was cast (see column 11). As to claims 43, 56, and 57, Sparkes et al. teach that the plasticizer is added in a quantity between 0 and 40% by total weight of the formulation

As to the separate addition of the polycarbonic acid as recited in instant claim 36, Sparkes et al. do not teach that the acid is separately added to the gelatin after being added to the chitosan. However, the order of this step for incorporating the acid into the reaction mixture for dialyzing chitosan and gelatin together is rendered obvious in view of the method for making a wound dressing material as taught by Sparkes et al. MPEP

2144.04 states as follows the legal precedent as a source for supporting obviousness rationale regarding changes in the sequence of adding ingredients:

> Ex parte Rubin , 128 USPQ 440 (Bd. App. 1959) (Prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.). See also In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to adjust the method steps as taught by Sparkes et al. for the dialysis of gelatin and chitosan. One would have been motivated to do so to optimize the yield of the target product and would have expected continued success from this adjustment since both processes are related to the dialysis of gelatin and chitosan with lactic acid, all components being present in aqueous reaction mixture.

Claims 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986) as applied to claims 36, 37, 42, and 55-57 above and as evidenced by C.G. B. Cole ("Gelatine: Its properties and its applications in dairy products" Dairy Symposium, 2001).

The teachings of Sparkes as they pertain to claims 36 and 37 are delineated above. As to claim 38, it is evidenced by C.G.B. Cole that gelatin type A and gelatin type B differ according to their source (pig skin or bones vs. cow hide or bones) and

according to their respective processes of isolation (treatment in alkali vs. treatment in alkaline media), however both share a molecular formula potentially differing only by molecular charge. Both types of gelatin are known to have gel properties, the strength of which are a function of bloom strength rather than starting material. Therefore, regardless of gelatine type A and gelatine type B's respective processes for production, these materials have equivalent chemical structures and known functional equivalence. As to claim 39, it is noted that the gelatin used was Bloom #250.

Therefore and as presented above, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to adjust the method steps as taught by Sparkes et al. for the dialysis of gelatin and chitosan. One would have been motivated to do so to optimize the yield of the target product and would have expected continued success from this adjustment since both processes are related to the dialysis of gelatin and chitosan with lactic acid, all components being present in aqueous reaction mixture.

Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986) as applied to claims 36, 37, 42, and 55-57 above, and further in view of McCarthy et al. (US 7,731,403 B2, filed Dec. 23, 2003).

The teachings of Sparkes et al. are delineated above. Sparkes et al. does not limit the molecular weight of the chitosan used.

However, McCarthy et al. teach wound dressings formed of a biomaterial comprising chitosan and a hydrophilic polymer. In these formulations, Sparkes et al. teach the preferred weight average molecular weight of chitosan to be at least about 150 kDa and most preferably at least about 300 kDa, a range overlapping with that instantly claimed.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to implement the preferred molecular weight chitosan as taught in the wound dressing materials of McCarthy et al. into the wound dressing materials of Sparkes et al. One would have been motivated to do so since McCarthy et al. teach that lower molecular weight chitosan wound dressings are unsuitable for patch applications since they are susceptible to dissolution upon contact with bodily fluids (see column 28, lines 56-59).

Claims 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986) and as evidenced by C.G. B. Cole as applied above, and further in view of Nordquist et al. (US 5,747,475, patented May 1998).

The teachings of Sparkes et al. are delineated above. Sparkes et al. do not specify the volume ratio or time for dialysis against water.

Nordquist et al. teach chitosan-derived biomaterials which result from the addition of a monosaccharide or oligosaccharide side chain to the free amino groups of the chitosan materials where the chitosan-derived biomaterials are useful in biomedical

applications including skin substitutes, sutures, dressings, and bandages for burns, wounds, and surgical procedures (see abstract, in particular; see also, column 13, lines 47-51). For example, the chitosan and the mono- or oligo-saccharide are mixed together and stirred for 24 hours at room temperature prior to subsequent steps and dialysis (see column 9, lines 31-column 10, line 10). Then, the suspensions (3 grams of saccharide plus one gram of chitosan, the product divided into three separate dialysis bags) are dialyzed overnight against 3.5 gallons of distilled water; then the bags are placed in fresh distilled water and dialysis is continued for an additional 7 hours (see column 10, lines 2-7).

It is the Examiner's position that the volume ratio and dialysis time are result effective variables because changing these variables clearly will affect the type of product obtained. See MPEP 2144.05 (b). Case law holds that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." See *In re Bosch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980). In view of this, it would have been obvious to one of ordinary skill in the art to utilize an appropriate volume ratio of polymer solution to water and a dialysis time, based on the teaching of Nordquist et al., including those within the scope of the present claims, so as to produce desired end results, particularly as they relate to the desired purity of the isolated product. Further, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to implement the method of modifying chitosan with saccharides as taught by Nordquist et al. into the materials comprising chitosan and gelatin as taught by Sparkes et al. One would have been motivated to do

so in order to achieve the solubilization of the chitosan and therefore the improved stabilization of chitosan gels and solutions as taught by Nordquist et al. (see column 9, lines 1-12).

Claims 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986) as applied above, and further in view of Ozmeric et al. ("Chitosan film enriched with an antioxidant agent, taurine, in fenestration defects", Journal of Biomedical Materials Research, Volume 51, Issue 3, p 500-503, published online June 2000).

The teachings of Sparkes et al. are delineated above. Sparkes et al. do not teach the addition of a polyfunctional amino acid as in instant claims 46 and 47.

However, Ozmeric et al. teach chitosan films having nontoxic, bioabsorbable, hemostatic, and antibacterial effects wherein taurine is implemented. Taurine is implemented into the films at 5% concentration, a value lying within the range recited in claim 48 (see page 501, column 1, paragraph 3 of "Materials and Methods").

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to implement taurine into a chitosan film as taught by Ozmeric et al. into the chitosan film dressing taught by Sparkes et al. One would have been motivated to do so in order to implement taurine's beneficial capability of regulating the inflammation process (see abstract, in particular) and protecting tissues against deleterious effects of oxidants (see introduction) since these benefits would

have served to improve the wound healing properties associated with the chitosan films and wound dressings (see introduction of Ozmeric).

Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986) as applied above, and further in view of Sagar et al. (US 4,960,413, patented Oct. 1990).

The teachings of Sparkes et al are delineated above. Sparkes et al. do not teach a bifunctional cross-linking agent as in the instant claim.

Sagar et al. teach a wound dressing comprising chitin and chitosan wherein active agents such anti-bacterial agents may be incorporated (see abstract, in particular). As to claim 49, Sager et al. teach that glutaraldehyde may be added to the wound dressings for its role as a bi-fuctional cross-linking agent (see column 1, lines 43-45).

It would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to incorporate the wound dressing agents (i.e., crosslinking agent, anti-bacterial agent) as taught by Sager et al. into the method of making wound dressing products as taught by Sparkes et al. One would have been motivated to do so to impart the improved strength associated with the glutaraldehyde bi-functional cross-linking agent (see Sager, column 1, line 44) or the anti-bacterial benefits as taught beneficial by Sager et al.

Claims 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986) as applied above, and further in view of Bloor (WO 2004/052413 A1, filed Dec. 5, 2003).

The teachings of Sparkes et al. are delineated above. Sparkes et al. do not teach the superoxide dismutase and/or catalase agents as in the instant claims.

However, Bloor teaches wound dressings containing an enzyme therapeutic agent (see abstract, in particular). Bloor teaches that the catalase enzyme may be added to the wound dressing materials (see paragraph [0026]). As to claim 51, Bloor teach that it is preferable that the amount of catalase used is about 0.01 ng to about 10 ng/gram of the dressing material, and a particular example teaches that a lactate oxidase/catalase conjugate was employed in an amount of 0.01 units each per part of collagen (see example 2, paragraph [0044]).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to incorporate and optimize the catalase enzyme as taught by Bloor into the wound dressing material of Sparkes et al. One would have been motivated to do so in order to accelerate the reduction of hydrogen peroxide into water and molecular oxygen, thereby improving the oxygen flow to the surface of the skin upon application of the dressing, and ultimately facilitating optimized wound healing processes (see also, paragraph [0027]).

Claims 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986) as applied above, and further in view of Peshoff (US 6,660,306 B2, patented Dec. 9, 2003).

The teachings of Sparkes et al. are delineated above. Sparkes et al. does not teach the addition of beta-carotene as in instant claims 52-54.

However, Peshoff teaches beta-carotene, among other Vitamin A forms, as an active agent in an antimicrobial and therapeutic wound healing composition active agent which may be topically applied (see abstract, in particular; see also claims 1 and 2, column 35; see also, column 7, lines 29-37). In addition, in one form of the invention, the therapeutic wound healing composition comprising the vitamin A active agent is incorporated into a pharmaceutical appliance in the form of sutures, staples, gauze, bandages, burn dressings, artificial skins, liposome or micelle formulations, etc. (see column 13, lines 31-36). Peshoff does not teach an embodiment of the invention employing beta-carotene in particular as the antioxidant in a therapeutic formulation, and for this reason this rejection is made using obviousness rationale. As to claim 54, Peshoff teaches that a preferred embodiment encompasses the antioxidant present in an amount from about 0.1 to about 40%, a range nearly overlapping with that recited in the instant claim. MPEP 2144.05 addresses as follows the patentability of overlapping ranges: "Similarly, a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)."

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to implement the carotene form of a vitamin A active agent as taught in the wound healing compound of Peshoff into the wound dressing material of Sparkes et al. One would have been motivated to incorporate the beta-carotene antioxidant into the formulation thereby facilitating absorption of the carotene into the cellular membrane to neutralize oxygen radicals, protecting the membrane, and improving the renewed skin growth. Based on the prior teaching of Peshoff, the skilled artisan reasonably would have expected continued success from this incorporation.

Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986) as applied above, and further in view of Lang (US 5,445,604, patented Aug. 1995).

The teachings of Sparkes et al. are delineated above. Sparkes et al. does not disclose the particular antibacterial substances in a particular quantity as recited in claim 56.

Lang teaches wound dressing materials with a wound contact layer having chlorhexidine active agent implemented in the embodiments of the invention. Example 9 teaches 1 g of chlorhexidine hydrochloride powder, which represents 0.02% by mass of the total 51 gram formulation (based on the components named in Example 2 to which Example 9 refers).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to incorporate the chlorhexidine antibacterial agent as

taught in the wound dressing materials of Lang in to the wound dressing materials of Sparkes et al. One would have been motivated to do so in order to incorporate the known antibacterial benefits of chlorhexidine (as taught by Lang) thereby improving the wound healing capabilities while minimizing undesirable bacterial presence in the wound dressing materials of Sparkes et al.

Claims 43 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sparkes et al. (US 4,572,906, patented Feb. 1986) as applied above, and further in view of Motosugi et al. (US 4,699,135, patented Oct. 1987).

The teachings of Sparkes et al. are delineated above. Sparkes et al. does not disclose the excipients recited in claim 58.

However, Motosugi et al. teach a shaped chitin body particularly effective as a wound dressing in which polyvinyl alcohol is implemented (see abstract, in particular; see also, comparative example 2, column 9, lines 51-58).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to implement polyvinyl alcohol as taught in the chitin materials of Motosugi et al. into the wound dressing materials of Sparkes et al. One would have been motivated to do so in order to improve the stability of the final product by implementing polyvinyl alcohol which Motosugi et al. teach acts as a binder (see column 5, line 43).

As to claim 43, neither Sparkes et al. nor Motosugi et al. teach the specified ratio of polycarbonic acid (lactic acid) to high molecular substance (polyvinyl alcohol, for example, as defined in the instant specification).

However, upon the prima facie obvious combination of Sparkes and Motosugi et al., the skilled artisan would have arrived at a formulation having the instantly prescribed ratio. For example, comparative Example 2 of Motosugi et al. teaches 0.05 grams of polyvinyl alcohol powder to 0.5 grams of dry chitosan fibers, and Sparkes et al. teaches 0.05 polyvinyl alcohol to 0.5 chitosan (see Table II, batch #236 in which the ratio of components is 10 gelatin, 9 chitosan, and 2 glycerol; lactic acid (second entry from bottom)). The combination of these teachings and therefore the implementation of lactic acid into the formulation having polyvinyl alcohol and chitosan would result in a combination having roughly a 2:1 ratio as in the instant claim. From the combination of teachings, the skilled artisan would have been motivated to optimize the resulting formulation in order to control the properties of the product, as is routine in the art.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AUDREA J. BUCKLEY whose telephone number is (571)270-1336. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/AJB/

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